Remarks

Claims 1-13 and 16-23 were pending in this application. Claim 12 has been amended for form. Claim 22 has been amended to limit the method to the treatment of cancer. Support for this claim can be found in the specification on page 5, lines 19-21, and on page 9, line 20 to page 10, line 14. Applicants reserve the right to pursue any additional subject matter in a continuation application.

As requested by the Examiner, an Abstract has been provided, the header "BRIEF DESCRIPTION OF THE DRAWINGS" has been added, and TABLE 2 has been moved from page 14 to page 11.

No new matter is introduced by these amendments. After entry of this amendment **Claims 1-13 and 16-23 are pending in this application**. Consideration of the pending claims is requested.

***Claim Rejections under 35 U.S.C. §112, 1st paragraph*:**

Claim 22 and dependent Claim 23 have been rejected under 35 U.S.C. §112, 1st paragraph because the specification, while being enabling for the treatment of cancer, allegedly does not provide enablement for treating any disorder or disease. Applicants respectfully disagree with this assertion.

However, solely to advance prosecution, Claim 22 has been amended to be limited to "a method for treating a cancer in an animal subject." This claim amendment is supported by the specification, *e.g.*, at page 5, lines 19-21, and from page 9, line 20 through page 10, line 14. Applicants note that the Office Action at page 2, paragraph 5 states that the specification is enabling for the treatment of cancer. In view of this amendment, Applicants request that the rejection be withdrawn.

Claim Rejections under 35 U.S.C. §102(b):

Claims 1-4, 6-13, and 16 have been rejected under 35 U.S.C. §102(b) as being allegedly anticipated by International Patent No. WO 98/56424A. Applicants traverse this rejection and request reconsideration.

Independent Claims 1 and 16 are both directed to polymer drug conjugates that comprise "a dextrin polymer, wherein said dextrin polymer is modified by succinoylation by at least 20mol%." As noted in the Office action (see page 3, paragraph 5), WO 98/56424A does not disclose a polymer drug conjugate that has been succinolylated to at least 20mol%. Thus, Applicants submit that independent Claims 1 and 16 are novel in view of WO 98/56424A. Claims 2-4 and 6-13 depend from Claim 1, and so are novel in view of WO 98/56424A, as well. Reconsideration and withdrawal of the rejection is respectfully requested.

Claim Rejections under 35 U.S.C. §103(a):

Claims 1-13 and 17-23 have been rejected under 35 U.S.C. §103(a) as being allegedly unpatentable over International Patent No. WO 98/56424A. Applicants respectfully traverse this rejection and request reconsideration.

WO 98/56424A relates to polymer drug conjugates of anti-cancer drugs that include dextrin, which is modified by the provision of a succinoyl linker group. The drug can be linked via the succinoyl group to dextrin. Dextrin with 1mol% and 5mol% succinoylation are disclosed to provide improved delivery.

However, WO 98/56424A does not disclose or render obvious the finding that the addition of pendant succinoly groups to a dextrin polymer drug conjugate increases the stability of the drug conjugate *in vitro*. Indeed, increasing stability is not discussed in WO 98/56424A. The reference does not appear to identify the problem being solved (increasing stability), and therefore could not be perceived to suggest the claimed solution. The prior art discloses attempts to modify dextrins by succinoylation, and discloses that varying temperature could be used to succinoylate dextrin up to 6.64% (see table 2, pate 10). Conjugation of doxorubicin to succinoylated dextran is disclosed using dextrin that is succinoylated between 0.5% to 14 mol%

(see Table 3, page 11). Since there is no suggestion of the need to increase the stability of the compounds, one of skill in the art would not be motivated to change the chemical nature of the biologically active molecules to overcome the problem. Thus, the prior does not suggest, nor provide motivation for, increasing the mol% of succinoylation to more than 20 mol% in order to increase stability.

Example 2, Figure 1, and Figure 2 of the present application provide a comparison of native dextrin, dextrin with 5mol% succinoylation, dextrin with 15mol% succinoylation, and dextrin with at least 20mol% succinoylation. Native dextrin, dextrin with 5mol% succinoylation, and dextrin with 15mol% succinoylation are rapidly degraded, whereas dextrin with at least 20mol% succinoylation (*e.g.*, 34mol% succinoylation) is markedly more stable *in vitro*.

Similarly, Example 3, Example 4, Figure 3, and Table 2 of the present application demonstrate that dextrin-doxorubicin that is more than 20mol% succinoylated (*e.g.*, 34mol% succinoylated dextrin-doxorubicin) is markedly more stable *in vivo*, and results in a superior and less toxic anti-tumor agent than does doxorubicin hydrochloride. WO 98/56424A does not disclose or render obvious the finding that the addition of pendant succinoly groups to a dextrin polymer drug conjugate increases the stability of the drug conjugate *in vivo*. Once again, increasing stability of the dextrin polymer drug conjugate is not discussed in WO 98/56424A.

Moreover, it is apparent that the advantageous increase in polymer stability by succinolylation has utility with respect to dextrin when used as an imaging agent. Examples 5-7 and Figures 5 and 6 of the present application demonstrate that increasing succinoylation of ^{125}I-labelled dextrin to greater than 20mol% improves the biodistribution of the dextrin. In particular, 34mol% succinoylated ^{125}I-labelled dextrin provides particularly good biodistribution. International Patent No. WO 98/56424A does not suggest nor render obvious the finding that dextrin that has been succinolylated to at least 20mol% confers these advantages.

Therefore, the present specification demonstrates that dextrin with at least 20mol% succinoylation provides unexpectedly superior results over dextrin alone or dextrin with 1mol%

or 5mol% succinoylation, and therefore overcomes any *prima facie* case of obviousness. Thus, Applicants respectfully request that this rejection of Claims 1-13 and 17-23 be withdrawn.

In conclusion, it is respectfully submitted that the present claims are in condition for allowance. If it may further issuance of these claims, the Examiner is invited to call the undersigned at the telephone number listed below.

Respectfully submitted,

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